LAST UPDATE: 02 August 2020

CORONAVIRUS
UPDATE
34

What we know about the COVID-19 immune response

THE LATEST ON COVID-19 IMMUNITY & THE CURRENT GLOBAL SITUATION

World Health Organization | EPI·WiN | infodemic MANAGEMENT

Overview

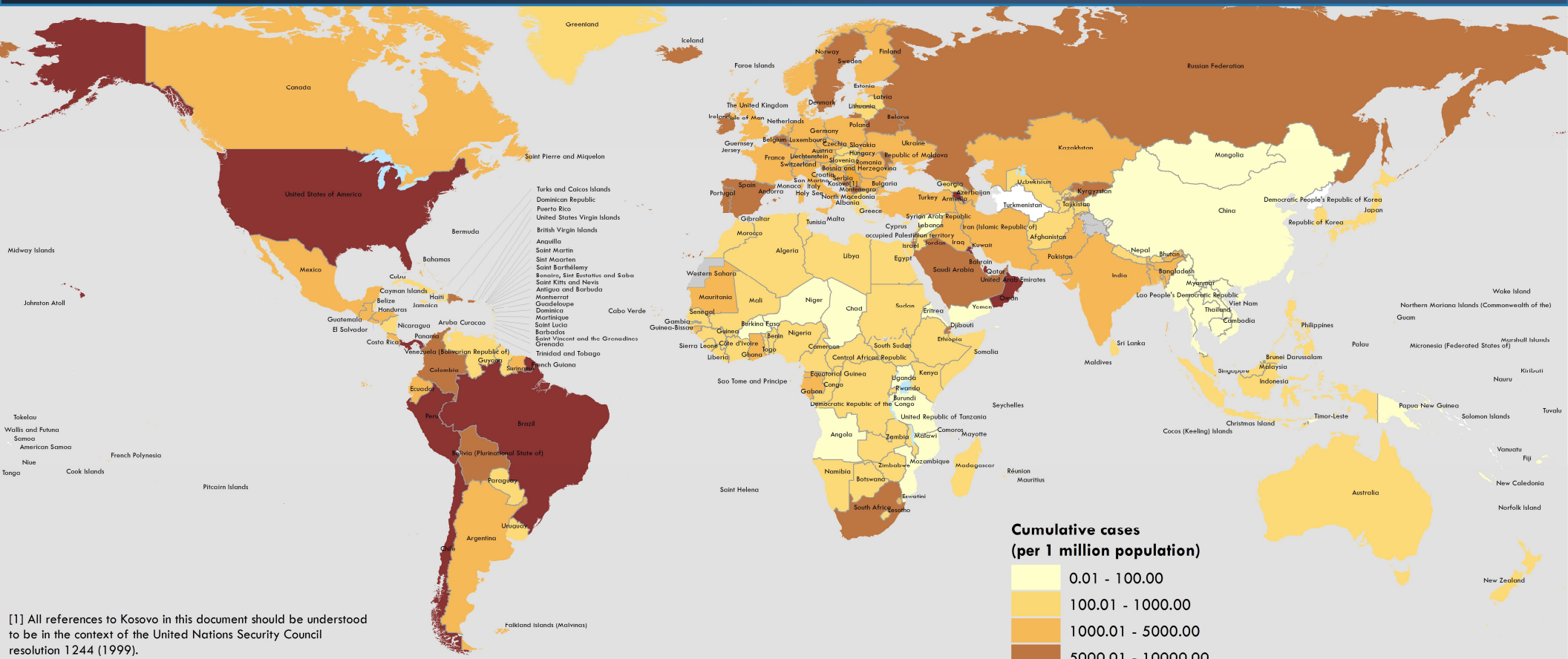
Current global situation
02 August 2020

- **> 17 million cases**
- 5 countries with highest cumulative number of cases
  - United States of America
  - Brazil
  - India
  - Russian Federation
  - South Africa

- **> 680,000 deaths**
- 5 countries with highest cumulative number of deaths
  - United States of America
  - Brazil
  - The United Kingdom
  - Mexico
  - India

COVID-19 cases per 1 million population

(AS OF 02 AUGUST 2020 10:00AM CEST)



[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

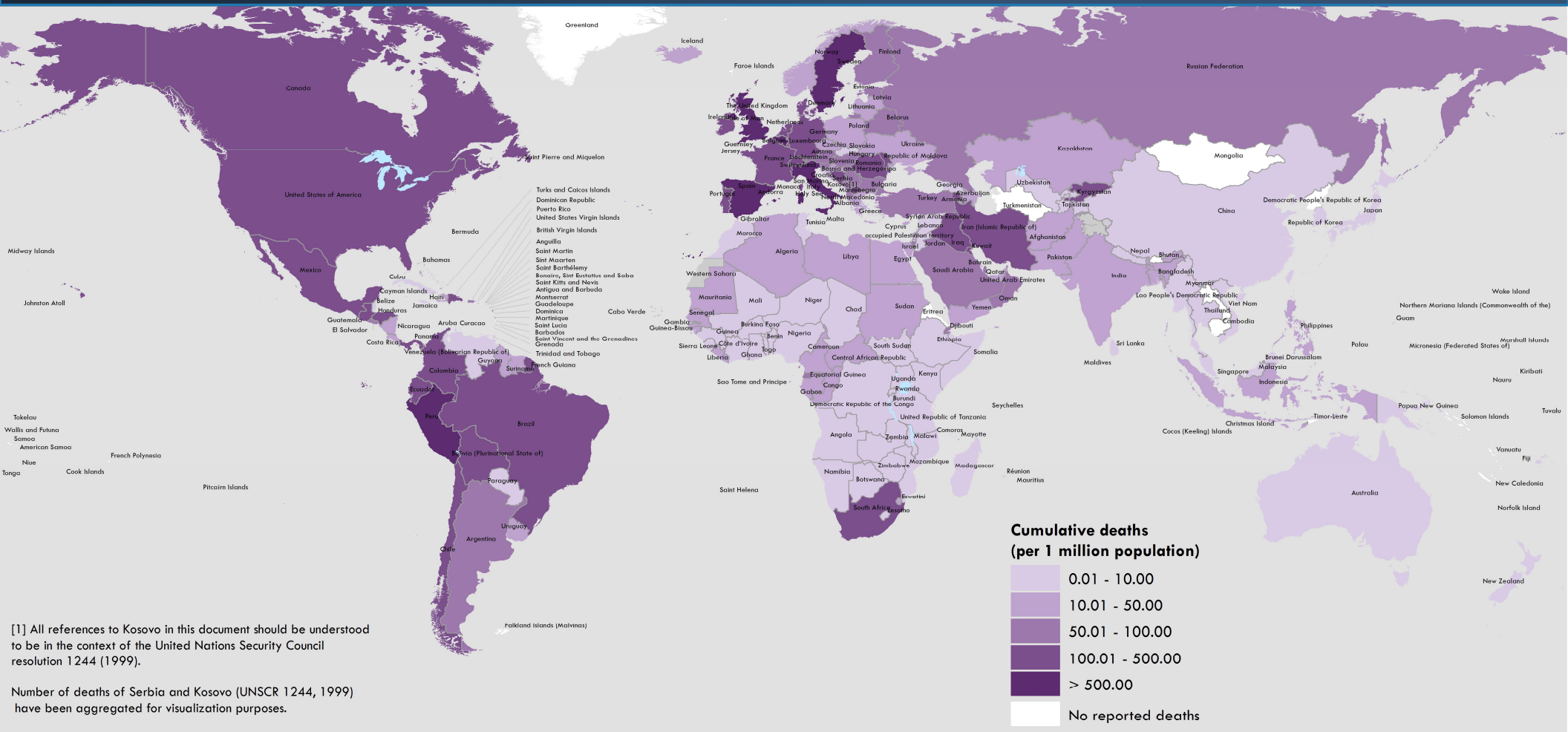
Number of cases of Serbia and Kosovo (UNSCR 1244, 1999) have been aggregated for visualization purposes.

***Data Source**: World Health Organization,*
United Nations Population Division (Population prospect 2020)
***Map Production**: WHO Health Emergencies Programme*

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

COVID-19 deaths per 1 million population

(AS OF 02 AUGUST 2020 10:00AM CEST)



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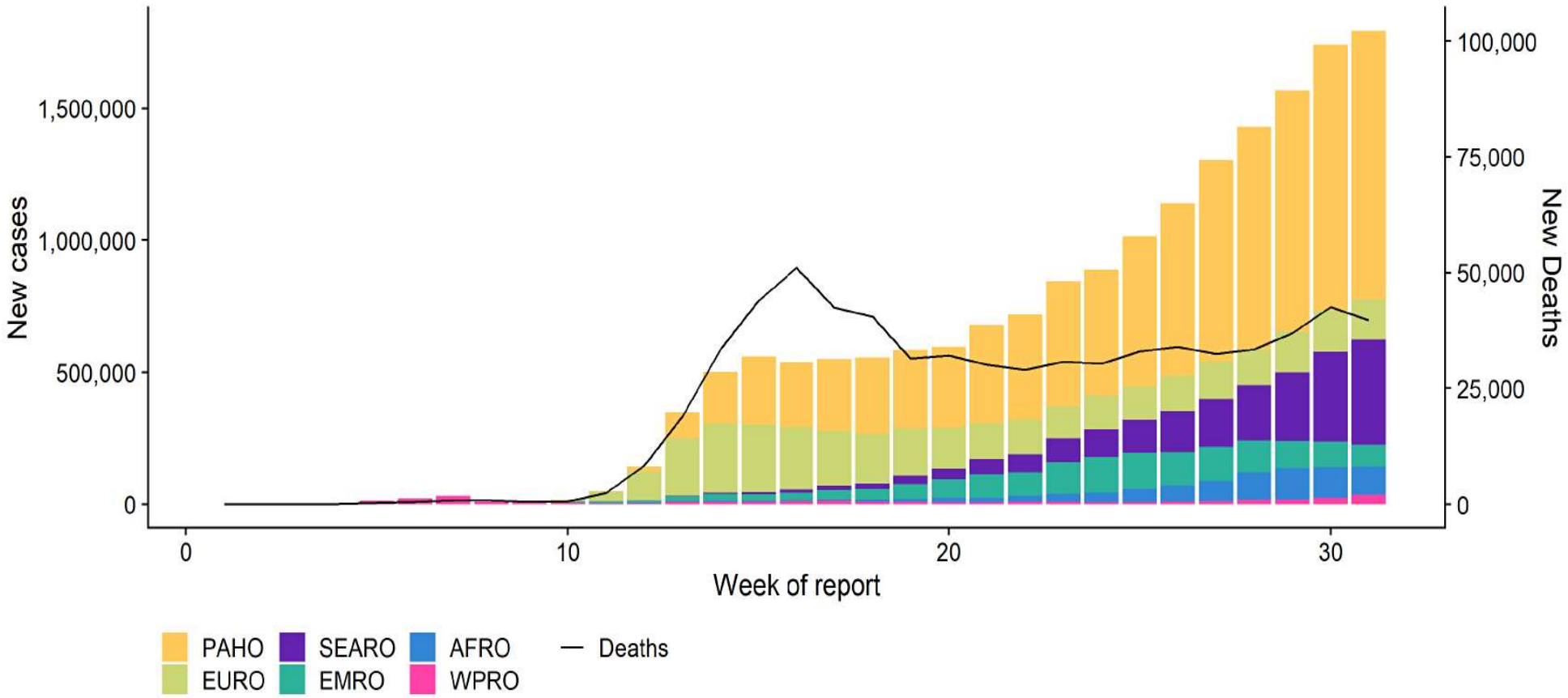
Global epidemic curve by region

(cases reported to WHO as of 02 August 2020)

NUMBER OF NEW CONFIRMED COVID-19 CASES & DEATHS BY WEEK

TOTAL 02 AUGUST: **17,660,523** CASES & **680,894** DEATHS



The immune response to viral infections

INFECTION CAN BE STOPPED AT THIS STAGE

PHASE ONE → PHASE TWO

Innate immune response

- General response to ANY infection
- Innate immune response cells secrete interferons[1] and other chemicals (cytokines)
- Interferons interfere with virus replication
- Phase 2 is triggered[2]

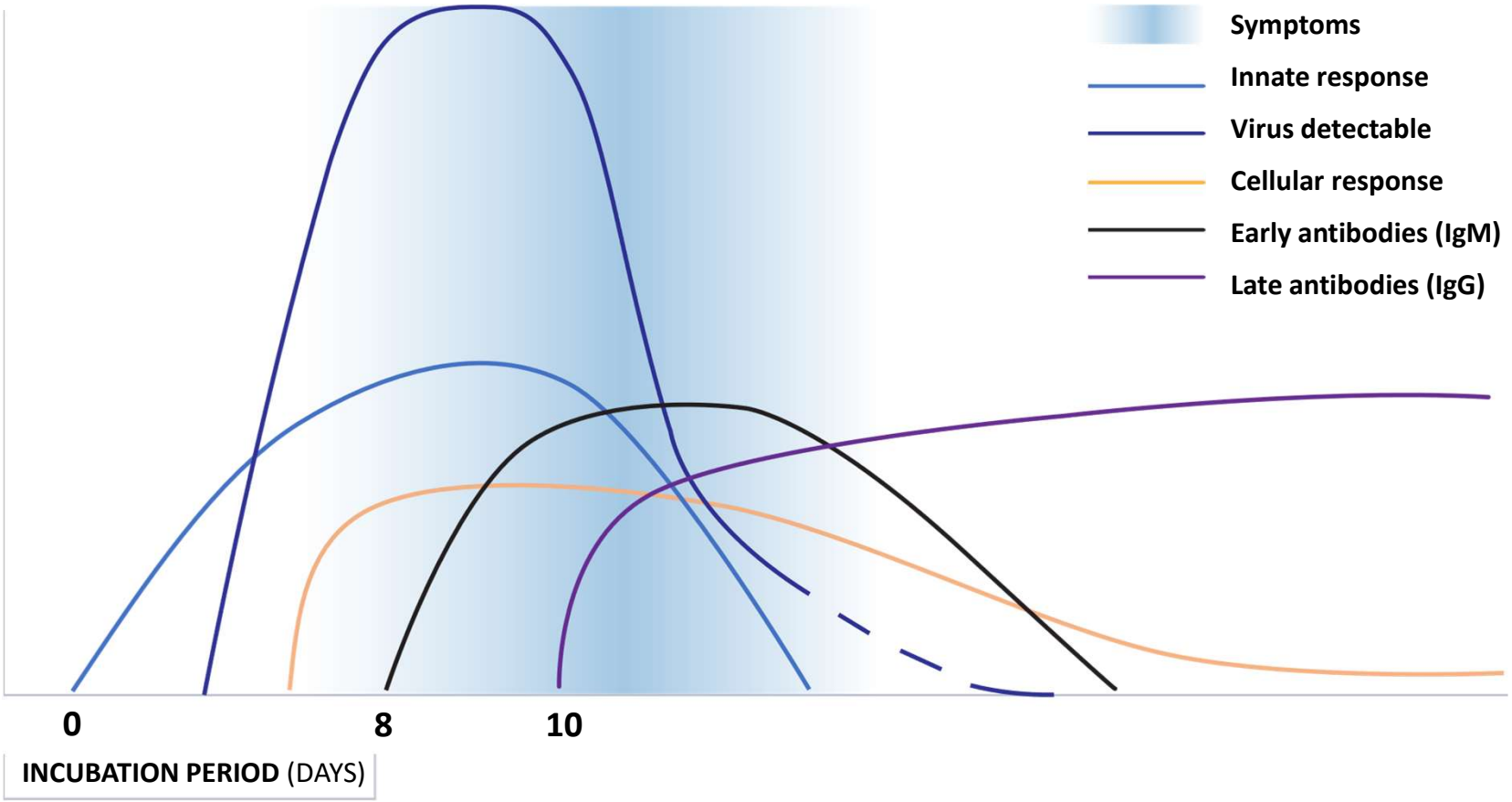
Adaptive immune response

- Specific response to the infection
- Starts after 6 - 8 days
- Involves two types of white blood cells
  - T cells (cellular response)
  - B cells (antibody response)

[1] Interferons and cytokines cause fever, muscle aches, etc - the early symptoms of infection

[2] A 'weaker' innate response (e.g. in elderly people or those with underlying health problems) may result in delayed stimulation of the adaptive response.

The immune response to viral infections in general

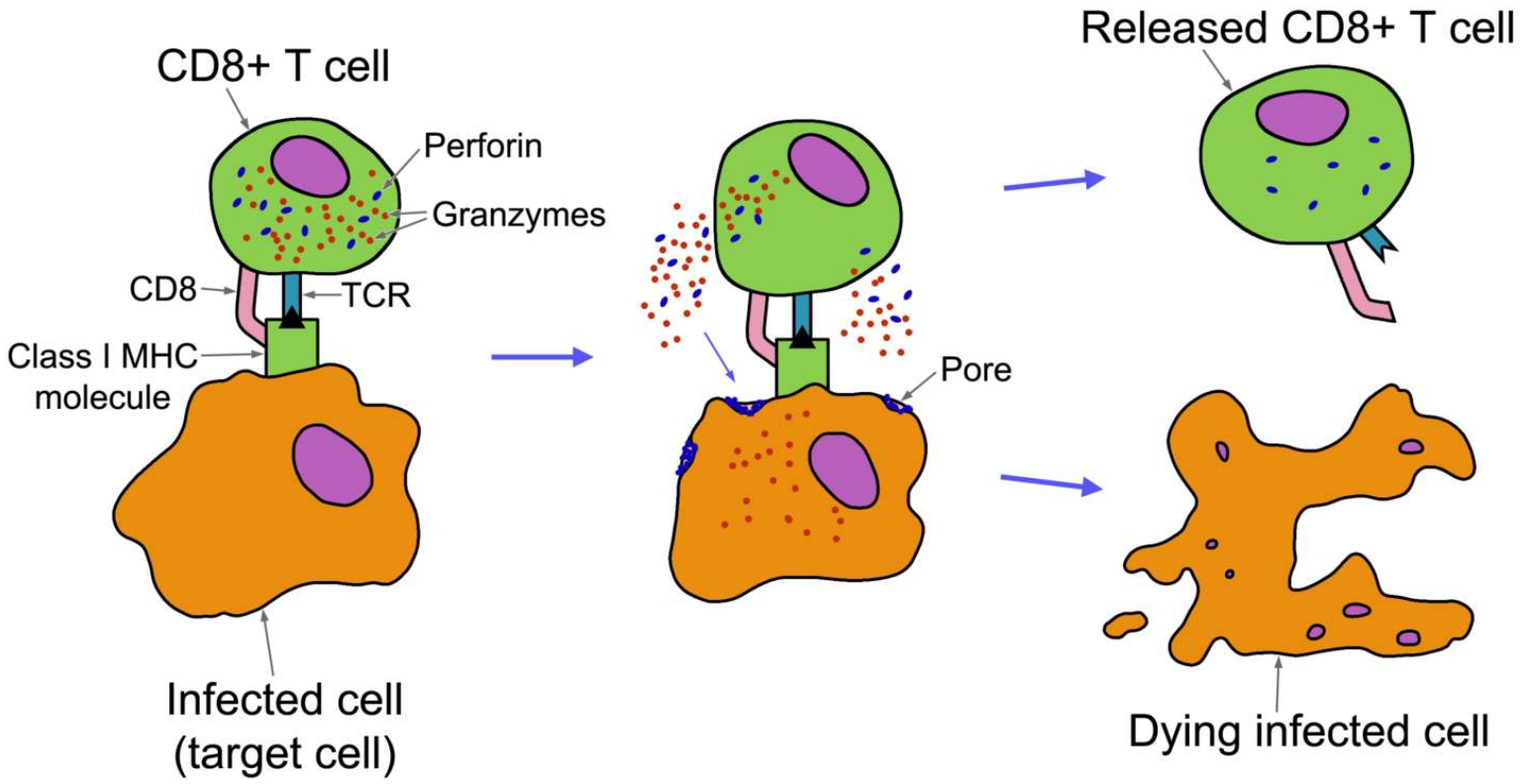


The adaptive response: T cells (start day 6 - 8)

T cells (cellular response)

- recognize cells that are infected with a specific virus and rapidly increase in number to tackle the infection
- types of T cells:
  - **CD8+ cytotoxic T cells** kill the cells in which the virus is multiplying and help to slow down or stop the infection.
  - **CD4+ helper T cells** bring in other cells of the immune system and stimulate B-Cells to produce antibodies specific to that virus.

CD8+ T cell destruction of virus-infected cells



TCR : T cell receptor; MHC: major histocompatibility complex

For further information, see source: Wikimedia Commons

The adaptive response: B cells (start day 6-8)

B CELLS (Antibody response)

- produce antibodies that are specific to that virus.
- IgM antibodies are produced first and disappear after a few weeks.
- IgG antibodies are produced at the same time or 2-3 days later, and titres (levels) usually remain for months or years.

MEMORY CELLS

- Once the infection is over, the T cells and B cells decline in number, but some cells will remain (memory cells)
- Memory cells respond rapidly if they come in contact with the same virus again, killing the virus and accelerating an antibody response.

The adaptive response: B cells (start day 6 - 8), cont.

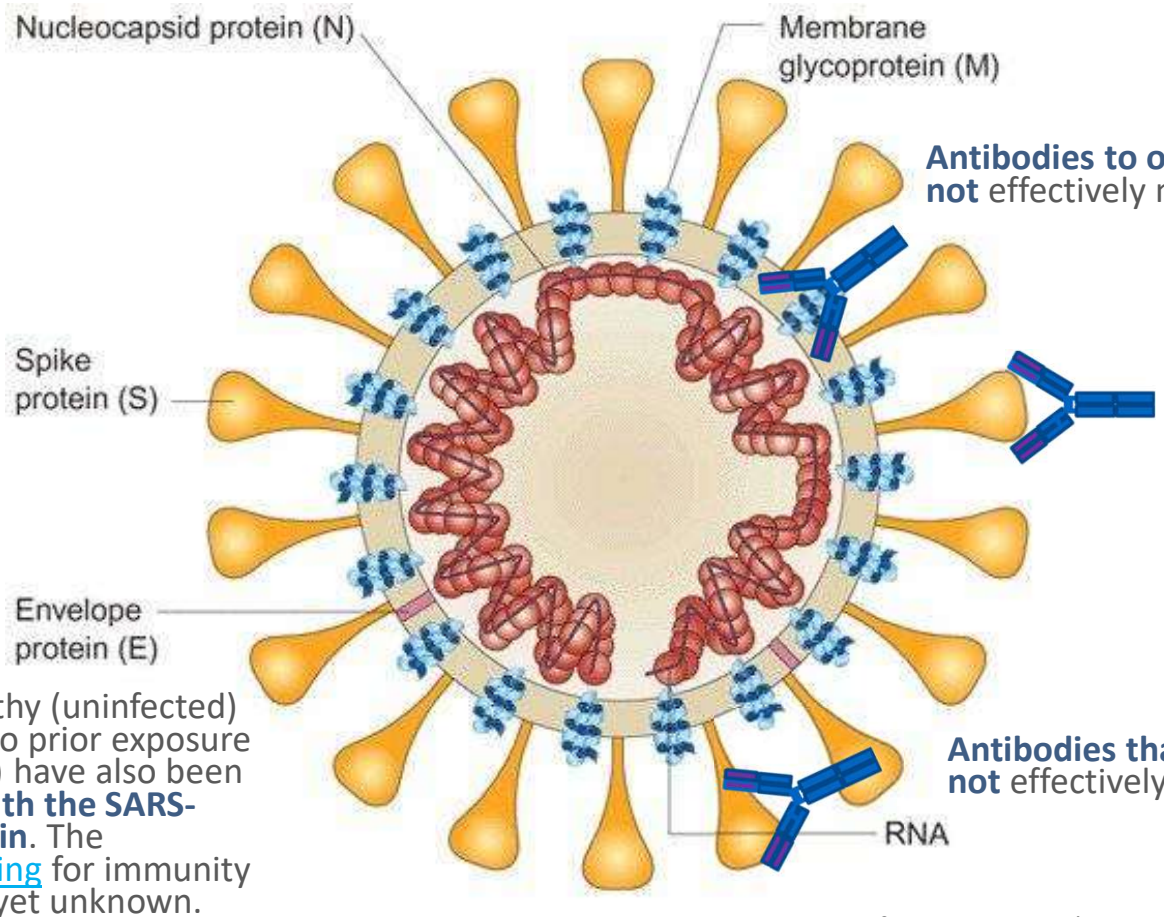
CRITICAL ASPECTS OF ANTIBODIES (Abs)

- **Quality:** do the Abs neutralize the virus (block it entering cells and multiplying)?
- Abs develop against different proteins that are part of a virus. Abs against one type of viral protein might neutralize the virus, while others might not.
- **Quantity:** how many antibodies are produced (titre)?
- **Duration:** how long do the antibodies persist in the body after infection?

CRITICAL ASPECTS OF VIRAL PROTEINS (Antigens)

- **Antigen stability:** Viruses may mutate over time. Viral proteins may change so much that antibodies produced against the virus won't recognize the antigens if they meet again later. (The importance of this phenomenon is not yet known for COVID-19)

Components of the SARS-CoV-2 virus: neutralizing antibodies bind to viral proteins



Antibodies to other components may not effectively neutralize the virus

Neutralizing antibody hypothesis: the antibody changes the viral spike protein and prevents entry of the virus via the ACE2 receptor into a targeted cell

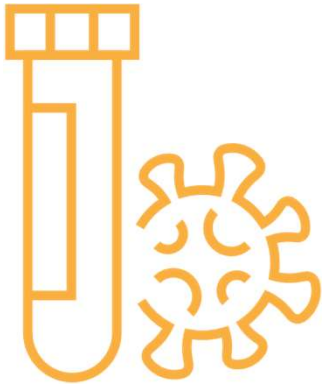
Antibodies that attach differently may not effectively neutralize the virus

** Some T cells in healthy (uninfected) persons (possibly due to prior exposure to other coronaviruses) have also been found to **cross-react with the SARS-CoV-2 viral spike protein**. The importance of this finding for immunity or vaccine design is as yet unknown.

Sources for hypothesis (5 June 2020) and image (16 July 2020)

Tests for COVID-19: the difference between molecular testing & serologic testing

- **Molecular testing, i.e. a PCR test,** detects genetic material of the virus and can detect if a person is currently infected with the COVID-19 virus.
- **Serologic testing** detects antibodies against the virus, which may indicate if a person had an infection with the virus that causes COVID-19 in the past.
- Most antibody tests cannot differentiate **neutralizing vs non-neutralizing antibodies**.
- **Rapid antibody detection tests** do not measure the titre (quantity) of antibodies.
- Other tests can provide the antibody titre, but may not distinguish between different kinds of antibodies (neutralizing vs non-neutralizing).



What does a positive antibody test tell us?

It tells us:

- ✓ The person was infected in the past with the virus that causes COVID-19
- ✓ If IgM and IgG are positive, infection was recent (i.e. within the past few weeks)
- ✓ If only IgG is present, the infection occurred more than a few weeks ago

It DOES NOT tell us:

- if the person has recovered (a persistent infection may be ongoing).
- if the antibodies are neutralizing (unless a specific assay is used).
- the antibody levels (unless a specific assay is used such as ELISA).

What does a negative antibody test tell us?

It could mean:

The person has not been infected

OR

The person was very recently infected (within the last 14 days)

OR

The person was infected and mounted an antibody response but the antibody levels are below the level of detection of the test

OR

The person was infected but cleared the virus without mounting an antibody response (not yet demonstrated for COVID-19)

Therefore, a negative antibody test does not tell us if a person is susceptible to infection.

What do we know about the immune response to COVID-19?

- Most COVID-19 patients who recovered have antibodies to the SARS-CoV-2 virus detectable in their blood.
- Most COVID-19 patients develop antibodies about 1-3 weeks after symptoms start. This is around the time when many patients start to recover.
- Patients who have had more severe disease appear to have **higher levels of important neutralizing antibodies**.
- Patients who had mild or asymptomatic COVID-19 have **low levels of neutralizing antibodies** (or even undetectable levels).
- In these persons it is possible the innate immune response and the T cell response cleared the virus
- Recent studies have shown that **neutralizing antibodies may disappear after 3 months**[1,2,3]

[1] https://www.nejm.org/doi/full/10.1056/NEJMc2025179 published 21 July 2020

[2] https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2768834 published 21 July 2020

[3] https://www.medrxiv.org/content/10.1101/2020.07.09.20148429v1.full.pdf published 11 July 2020

Does the presence of antibodies against COVID-19 mean a person is immune and protected from being infected again?

No one knows yet!

- Generally, a person who recovers from a viral infection is protected against new infection, if the antibodies are of adequate quality (neutralizing antibodies) and quantity (high levels)
- Changes in the virus sequence can make prior immunity less effective (eg. as happens with the influenza virus)
- Protection from re-infection with the common cold caused by other milder coronaviruses is short-term (sometimes less than a year)
- For other coronaviruses, such as Severe Acute Respiratory Syndrome (SARS), antibodies have been detected a few years later.

For COVID-19, we do not yet have enough data to confirm if antibodies protect, what antibody levels are required, or how long protection will last.

‘Herd immunity’ in the context of COVID-19

- **Herd immunity** is the indirect protection of individuals from an infectious disease when a high proportion of a population is immune (usually through vaccination). Persons who haven’t been infected, or who haven’t had a good immune response, are protected because there are enough immune people around them to slow or stop person-to-person transmission.
- Many countries are testing for COVID-19 antibodies in the population[1] or in specific groups[2].
- **Fewer than 10% of the general population have detectable COVID-19 antibodies** (excepting in a few high intensity transmission sites or in specific small groups).
- Worldwide **most people remain susceptible to COVID-19 infection**.

[1] Selected seroprevalence studies can be found here and here.
[2] Unity Studies: Early Investigation Protocols: *https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations*

What can serosurveys teach us about immunity?

- **Serological surveys** measure the proportion of the people in a community, group or population who have **detectable antibodies** to an infectious disease of interest

Questions that CAN be answered through serological surveillance and studies

- What % of the group or population have been infected with SARS-CoV-2?
- How is this changing over time?
- Are there specific characteristics, risk factors or protective factors associated with SARS-CoV-2 infection (age, place, pre –existing conditions, etc)
- What % of the group or population experienced mild COVID-19 illness or asymptomatic infection?
- For how long can antibodies be found after a COVID-19 infection?

Questions that CANNOT be answered through serological surveillance and studies

- What % of the group or population is immune to COVID-19 and cannot be infected again?
- How many antibodies (what titres or levels), are needed to protect someone from COVID-19?
- For how long will someone with antibodies be protected from COVID-19?
- Can someone be re-infected with COVID-19?
- Can knowledge of antibodies be used to group people together in settings such as schools, dormitories, and correctional facilities?

At the present time, there is no role for a COVID-19 ‘immunity certificate’

- Some have asked if the presence of antibodies to the virus that causes COVID-19 could serve as the basis for an **'immunity certificate’’** to enable individuals to travel or return to work.
- This rests on the as-yet unproven assumption that infection provides long-term protection against re-infection. Antibody-mediated immunity **is not yet sufficiently** understood to offer any guarantees of protection against re-infection.
- So **a positive antibody test cannot be used to exempt anyone from public health measures** in their community or at work or to group people in settings such as schools, dormitories, or correctional facilities.

There is currently insufficient information to conclude whether people who have recovered from COVID-19 and have antibodies are protected from a second infection.

How can we protect ourselves and others?

- **Stay home and self-isolate** if you feel unwell, even with mild symptoms
- **Clean hands frequently** with soap and water for 40 seconds or with alcohol-based hand rub for 20 seconds
- **Cover your nose and mouth** with a disposable tissue or flexed elbow when you cough or sneeze
- **Avoid touching** your eyes, nose and mouth
- Maintain a **minimum physical distance of at least 1 metre** from others
- **Stay away from crowds** and stay away from poorly ventilated indoor spaces
- **Use a fabric mask** where physical distancing of at least 1 metre is not possible
- **Use a medical / surgical mask** if you may be at higher risk (age, medical conditions)
- **Regularly clean and disinfect** frequently-touched surfaces

VIDEOS:

Transmission

How to break the chains of transmission

Protecting ourselves

How to protect yourself against COVID-19

Seven steps to prevent the spread of the virus

Masks

Medical and fabric masks: who wears what when?

How to wear a fabric mask safely

How to wear a fabric mask

How to wear a medical mask

Immunity through vaccination

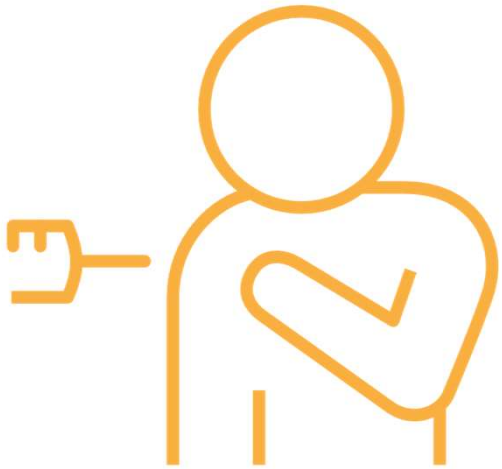
- **Vaccines safely deliver an immunogen** to the immune system to train it to recognize the pathogen when it is encountered naturally.
- The nature of the immunogen and route of administration affects the type of immune response induced, the safety, the protection and the duration of protection.

Immunogens:

- **Attenuated pathogen** (live, replicating, but not pathogenic)
- **Killed inactivated pathogen**
- **Subunit** (derived from pathogen)
- **Recombinant** (viral antigen produced in a host cell and purified)
- **Peptides** (synthetic fragments of antigen)
- **Vectored** (viral pathogen expressed on a safe virus)
- **Nucleic acid** (DNA or RNA coding for a viral protein and injected into body)

Route:

- **Injection** (in the muscle or under the skin), nasal spray, oral drops, aerosol



WHO guidance on COVID-19 immunity

Additional resources

- IMMUNITY PASSPORT
  https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19

- Q&A SEROLOGY
  https://www.who.int/news-room/q-a-detail/q-a-serology-and-covid-19

- VACCINE LANDSCAPE
  https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines

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- THE UNITY STUDIES: EARLY INVESTIGATIONS PROTOCOLS
  https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations

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Upcoming event:

International Youth Day Webinar

12 AUGUST 2020, 12:30 - 14:00 CET

Join youth from around the world, UNESCO Director-General Audrey Azoulay and WHO Director-General Dr Tedros Adhanom Ghebreyesus to discuss COVID-19 initiatives.

Q&A with WHO Director General - Dr Tedros Adhanom Ghebreyesus

Are you a young adult with a question for Dr Tedros?
Please send your questions to Katherine at epi-win@who.int

To join the webinar, please register in advance.

MORE INFORMATION

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